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(FILE 'HOME' ENTERED AT 09:57:20 ON 31 MAR 2003)

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SEA (G PROTEINS)

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L1 QUE (G PROTEINS)

FILE 'CAPLUS, ESBIOBASE, SCISEARCH, BIOSIS, MEDLINE, EMBASE, TOXCENTER, BIOTECHNO, LIFESCI, PASCAL, CANCERLIT' ENTERED AT 09:59:31 ON 31 MAR 2003

L2 3469 S L1 AND (BETA SUBUNIT)
L3 10 S L2 AND (TASTE)
L4 6 DUP REM L3 (4 DUPLICATES REMOVED)
L5 3 S L2 AND TONGUE
L6 3 DUP REM L5 (0 DUPLICATES REMOVED)
L7 4 S L2 AND (BITTER OR SWEET OR SOUR)
L8 3 DUP REM L7 (1 DUPLICATE REMOVED)

=> d l4 ibib ab 1-6

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:43370 CAPLUS
DOCUMENT NUMBER: 136:195743
TITLE: G.beta. association and effector interaction selectivities of the divergent G subunit G.gamma.13
AUTHOR(S): Blake, Bonita L.; Wing, Michele R.; Zhou, Janice Y.; Lei, Qiubo; Hillmann, Jennie R.; Behe, Cynthia I.; Morris, Rebecca A.; Harden, T. Kendall; Bayliss, Douglas A.; Miller, Richard J.; Siderovski, David P.
CORPORATE SOURCE: Department of Pharmacology, University of North Carolina Neuroscience Center, University of North Carolina, Chapel Hill, NC, 27599-7365, USA
SOURCE: Journal of Biological Chemistry (2001), 276(52), 49267-49274
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB G.gamma.13 is a divergent member of the G.gamma. subunit family considered to be a component of the gustducin G-protein heterotrimer involved in bitter and sweet **taste** reception in **taste** bud cells. G.gamma.13 contains a C-terminal asparagine-proline-tryptophan (NPW) tripeptide, a hallmark of RGS protein G.gamma.-like (GGL) domains which dimerize exclusively with G.beta.5 subunits. In this study, we investigated the functional range of G.gamma.13 assembly with G. **beta. subunits** using multiple assays of G.beta. assocn. and G.beta..gamma. effector modulation. G.gamma.13 was obsd. to assoc. with all five G.**beta. subunits** (G.beta.1-5) upon co-translation in vitro, as well as function with all five G.**beta. subunits** in the modulation of Kir3.1/3.4 (GIRK1/4) potassium and N-type (.alpha.1B) calcium channels. Multiple G.beta./G.gamma.13 pairings were also functional in cellular assays of phospholipase C (PLC) .beta.2 activation and inhibition of G.alpha.q-stimulated PLC.beta.1 activity. However, upon cellular co-expression of G.gamma.13 with different G.**beta. subunits**, only G.beta.1/G.gamma.13, G.beta.3/G.gamma.13, and G.beta.4/G.gamma.13 pairings were found to form stable dimers detectable by co-immunopptn. under high-detergent cell lysis conditions. Collectively, these data indicate that G.gamma.13 forms functional G.beta..gamma. dimers with a range of G.**beta. subunits**. Coupled with our detection of G.gamma.13 mRNA in mouse and human brain and retina, these results imply that this divergent G.gamma. subunit can act in signal transduction pathways other than that dedicated to **taste** reception in sensory lingual tissue.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:899022 CAPLUS
DOCUMENT NUMBER: 136:229948
TITLE: Acidic stimuli activates two distinct pathways in **taste** receptor cells from rat fungiform papillae
AUTHOR(S): Liu, Lieju; Simon, S. A.
CORPORATE SOURCE: Department of Anesthesiology, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Brain Research (2001), 923(1,2), 58-70
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A sour **taste** sensation may be produced when acidic stimuli interact with **taste** receptor cells (TRCs) on the dorsal surface of the tongue. We have searched for pathways in TRCs that may be activated by acidic stimuli using RT-PCR and changes in intracellular calcium (Ca2+I) induced by acidic stimuli in rat fungiform papillae. RT-PCR revealed the presence of proton-gated subunits ASIC-.beta. and VR1. Ca2+ imaging measurements of the TRCs revealed two distinct responses to acidic stimuli: Ca2+i was increased in 9% (28/308; Type I) and was decreased in 39% (121/308; Type II). Neither of these responses was affected by the removal of extracellular Ca2+, indicating that the changes arise from the release and sequestration of Ca2+ from intracellular stores. These responses were also not inhibited by the vanilloid receptor antagonist, capsazepine, suggesting they do not arise from the activation of vanilloid receptors. The Type I, but not the Type II response was inhibited by amiloride. Dose-response measurements for Types I and II responses yielded pH50% of 4.8 and 4.9, resp. Type II responses were inhibited by pertussis toxin, suggesting G-protein involvement. TRCs that exhibit Type II responses could also be activated by quinine (which increased Ca2+I) thus suggesting a mechanism by which the addn. of acid may be suppressive to other chem. stimuli.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:535372 CAPLUS

DOCUMENT NUMBER: 133:148114

TITLE: Assays for sensory modulators using a sensory cell specific G-protein **.beta. subunit**

INVENTOR(S): Zuker, Charles S.; Adler, Jon Elliot; Lindemeier, Juergen

PATENT ASSIGNEE(S): Regents of the University of California, USA

SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000045179	A2	20000803	WO 2000-US2218	20000126
WO 2000045179	A3	20001207		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-117404P P 19990127

AB The invention identifies nucleic acid and amino acid sequences of a sensory cell specific G-protein .alpha. subunit that are specifically expressed in sensory cells, e.g., **taste** cells, antibodies to such G-protein .alpha. subunits, methods of detecting such nucleic acids and subunits, and methods of screening for modulators of a sensory cell specific G-protein .alpha. subunit. A G protein specific to sensory cells, e.g. **taste** buds, is identified and the .alpha. subunit characterized and a cDNA encoding it is cloned. Measurements of G protein-induced activity, such as changes in intracellular cyclic nucleotides or calcium, inositol phosphates or diacylglycerols can be used to assay for modulators of the activity of these proteins. A rat cDNA for the subunit was cloned by screening cDNA libraries from gustducin-pos.

cells for G protein sequences.

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:647577 CAPLUS
DOCUMENT NUMBER: 133:320140
TITLE: G protein .beta..gamma. complexes in circumvallate **taste** cells involved in bitter transduction
AUTHOR(S): Rossler, Patricia; Boekhoff, Ingrid; Tareilus, Erwin; Beck, Stefan; Breer, Heinz; Freitag, Joachim
CORPORATE SOURCE: Institute of Physiology, University Stuttgart-Hohenheim, Stuttgart, D-70593, Germany
SOURCE: Chemical Senses (2000), 25(4), 413-421
CODEN: CHSED8; ISSN: 0379-864X
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB G protein .beta..gamma. (G.beta..gamma.) complexes are considered to play an important role in second messenger signaling of phospholipase C (PLC). Monitoring the inositol 1,4,5-trisphosphate (IP3) response in circumvallate tissue homogenates upon stimulation with denatonium benzoate, it was demonstrated that a glutathione S-transferase-GRK3ct fusion protein-a G.beta..gamma. scavenger-attenuates the bitter tastant-induced second messenger reaction. Towards an identification of the G.beta..gamma. complex involved in rat bitter **taste** transduction, it was found that the G protein .beta.3 subtype is specifically expressed in **taste** receptor cells of circumvallate papillae. G.beta.3-specific antibodies blocked the denatonium benzoate-induced IP3 formation in a dose-dependent manner; the inhibitory effect was reversed by preincubation with the antigenic peptide. A less pronounced inhibition was obsd. using G.beta.1-specific antibodies. Analyzing individual **taste** cells by single cell reverse transcriptase-polymerase chain reaction approaches, overlapping expression patterns for PLC.beta.2, G.alpha.gust, G.beta.3 and G.gamma.3 could be demonstrated. Furthermore, the coexpression of all profiled signal transduction components in individual **taste** receptor cells could be detected. These data support the concept that the denatonium benzoate-induced IP3 response is mediated by an activation of PLC.beta.2 via a G.beta..gamma. complex, possibly composed of G.beta.3 as the predominant .**beta**. **subunit** and G.gamma.3, and imply that multiple second messenger pathways may exist in individual **taste** receptor cells.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 6 LIFESCI COPYRIGHT 2003 CSA
ACCESSION NUMBER: 1998:113026 LIFESCI
TITLE: Cell growth control by G protein-coupled receptors: from signal transduction to signal integration
AUTHOR: Gutkind, J.S.
CORPORATE SOURCE: Oral and Pharyngeal Cancer Branch, National Institute of Dental Research, National Institutes of Health Bethesda, MD 20892, USA
SOURCE: Oncogene, (19980917) vol. 17, no. 11, Supp. 1, pp. 1331-1342. Reviews..
ISSN: 0950-9232.
DOCUMENT TYPE: Journal
TREATMENT CODE: General Review
FILE SEGMENT: B
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Many growth factors are known to bind and activate either receptors possessing an intrinsic protein-tyrosine kinase activity, or those that transmit signals to the cytoplasm through the interaction with heterotrimeric GTP-binding proteins (**G proteins**). The

latter are collectively known as G protein-coupled receptors (GPCRs) and comprise the largest group of cell surface receptors. With more than 1000 members, they represent more than 1% of the similar to 100 000 proteins encoded by the human genome. The best known family of GPCRs exhibit a common structural motif consisting of seven membrane-spanning regions. These receptors can be activated by a diverse array of external stimuli, including growth factors, vasoactive polypeptides, chemoattractants, neurotransmitters, hormones, phospholipids, photons, odorants, and **taste** ligands. Activation of GPCRs by these agents elicits a profound change in the transmembrane alpha helices, thus affecting the conformation of intracellular loops uncovering previously masked G protein binding sites. This causes the exchange of GDP for GTP bound to the G protein alpha subunit, and a conformational change in three flexible 'switch regions' of G alpha , activating G alpha and causing its dissociation from the beta gamma heterodimers. In turn, GTP-bound G protein alpha subunits or beta gamma complexes initiate intracellular signaling responses by acting on effector molecules such as adenylyl cyclases, phosphodiesterases, phospholipases, or regulating the activity of ion channels, ion transporters, and a growing number of kinases. To date, 16 distinct mammalian G protein alpha subunits have been identified, and divided into four families based upon sequence similarity: alpha sub(s), alpha sub(i), alpha sub(q), and alpha sub(12). In addition, 11-G protein gamma subunits and five G protein **beta subunits** have been cloned so far. Taken together, it is becoming increasingly clear that GPCRs represent one of the most diverse signal transduction systems in eukaryotic cells. The biochemical and biological consequences of this diversity in subunit composition have just begun to be appreciated. In this review, we will describe the role of GPCRs in normal and aberrant cell growth and will then focus on recent efforts aimed to elucidate their downstream intracellular signaling pathways controlling cell proliferation.

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2

ACCESSION NUMBER: 1987:115453 CAPLUS
DOCUMENT NUMBER: 106:115453
TITLE: Interaction of GTP-binding regulatory proteins with chemosensory receptors
AUTHOR(S): Bruch, Richard C.; Kalinoski, D. Lynn
CORPORATE SOURCE: Monell Chem. Senses Cent., Philadelphia, PA, 19104, USA
SOURCE: Journal of Biological Chemistry (1987), 262(5), 2401-4
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB GTP-binding regulatory proteins (**G proteins**) were identified in chemosensory membranes from the channel catfish Ictalurus punctatus. The common G protein .**beta**.-**subunit** was identified by immunoblotting in both isolated olfactory cilia and purified **taste** plasma membranes. A cholera toxin substrate (mol. wt., Mr, 5,000), corresponding to the G protein that stimulates adenylate cyclase, was identified in both membranes. Both membranes also contained a single pertussis toxin substrate. In **taste** membranes, this component comigrated with the .alpha.-subunit of the G protein that inhibits adenylate cyclase. In olfactory cilia, the Mr 40,000 pertussis toxin substrate cross-reacted with antiserum to the common amino acid sequence of G protein .alpha.-subunits, but did not cross-react with antiserum to the .alpha.-subunit of the G protein from brain of unknown function. The interaction of **G-proteins** with chemosensory receptors was detd. by monitoring receptor binding affinity in the presence of exogenous guanine nucleotides. L-Alanine and L-arginine bind with similar affinity to sep. receptors in both olfactory and gustatory membranes from the catfish. GTP and a nonhydrolyzable analog decreased the affinity of olfactory L-alanine and L-arginine receptors by .apprx. 1 order of magnitude. In contrast, the binding affinities of the corresponding

taste receptors were unaffected. These results suggest that olfactory receptors are functionally coupled to G-proteins in a manner similar to some hormone and neurotransmitter receptors.